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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
| 08/803,702         | 02/21/97    | MAINO                 | V P-3639P1       |

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| EXAMINER |
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18M1/0916

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|            |              |
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| GAMBEL, P. |              |
| ART UNIT   | PAPER NUMBER |

1806

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DATE MAILED: 03/16/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

- ☐ Responsive to communication(s) filed on \_\_\_\_\_
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

- ☒ Claim(s) 1-18 is/are pending in the application.
- Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-18 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948. **SUBSTITUTE**
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449. Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948 **SUBSTITUTE**
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

### DETAILED ACTION

1. The drawings submitted with this application were declared informal by the applicant. Accordingly, they have not been reviewed by a draftsman at this time. When formal drawings are submitted, the draftsman will perform a review.

Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Applicant is reminded that changes to the Brief Description of the Drawings may be required to be in accordance with the above-mentioned review.

Photographs are not acceptable until petition is granted as set forth in 37 CFR 1.84(b). Under 37 CFR 1.84(b), the applicant must file a petition with fee requesting acceptance of the color and black and white photographs. The petition is decided in the Office of the Group Director.

2. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The specification is objected to and claims 1-18 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. In evaluating the facts of the instant case, the following is noted:

Applicant has not enabled measuring expression of one or more intracellular cytokines other than  $\gamma$ -IFN, IL-2, IL-4, IL-5, IL-10 and TNF- $\alpha$ ; measuring an early activation antigen other than CD69; or providing a costimulus other than via CD28, CD40, CD86 or CD118. The specification does not appear to specifically define the metes and bounds of "intracellular cytokines", "costimulus" or "early activation antigen" a costimulatory signal in the T cell". As such, these terms cannot be considered to be limited to the specific use of the specificities indicated above to determine antigen specific activation of T cells, as claimed or disclosed in the specification. It is not sufficient to define a specificity by its principal biological activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed cytokines, activation antigens or costimuli in manner reasonably correlated with the scope of the claims broadly including any number of costimulatory signals or specificities. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 C.F.R. § 102(f) or (g) prior art under 35 C.F.R. § 103.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation

8. Claims 1 and 3-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Picker et al. (Blood, 1995) (see entire document). Picker et al. teaches the method of determining the antigen specific activation of T cells of the instant invention. Picker et al. teaches the method of determining the antigen specific activation of T cells of the instant invention, including the claimed specificities and limitations. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention.

9. Claims 1-18 are rejected under 35 U.S.C. § 103 as being unpatentable over Picker et al. (Blood, 1995) in view of art known procedures to use cationic chelating agents in flow cytometry, as evidenced by Seon et al. (U.S. Patent No. 5,407,805), to lyse red blood cells, as evidenced by Schwartz (U.S. patent No. 5,093,234) and in view of art known motivation to detect antigen specific activation to a wide variety of antigens at the time the invention was made.

Picker et al. teach the instant claims are drawn to a method of determining the antigen specific activation of T cells including the claimed specificities and limitations.

Picker et al. differs from the instant methods by not teaching all of the claimed costimuli, however by teaching CD28, it would have led the ordinary artisan to apply other known T cell costimuli at the time the invention was made

Picker et al. differs from the instant methods by not teaching the art known lysis of RBCs and washing to remove debris from cell preparations for culture and FACS analysis, as evidenced by Schwartz and well-practiced at the time the invention was made, particularly with animal cells.

Picker et al. differs from the instant methods by not teaching the use of EDTA in washing cells, however this has long been used to prevent cell clumping and to reduce background in fluorescence, as known in the art at the time the invention was made or as evidenced by Seon et al. (U.S. Patent No. 5,407,805).

Picker et al. differs from the instant methods by teaching the term immunosuppressive or immunoaugmenting agent per se, however this reference does teach activation via PMA, ionomycin and superantigens. Also this reference discusses the broad importance of this assay in measuring and monitoring immune status. Therefore, it would have been obvious to the ordinary artisan to apply a number of immunomodulating agents, including both stimulatory and suppressive to the referenced system in analyzing immune functions of various cell populations at the time the invention was made.

Picker et al. differs from the instant methods by not teaching all of the antigens encompassed by the claims per se, however this reference refers to the manifestation of immunity either protective or pathologic depends on the functional activity of memory/effector T cell subsets. Also, the specification acknowledges that there were a number of assays known in the art to detect antigen specific activation of T cells and that the difference of the instant application is drawn to the multi parametric flow cytometry analysis. Therefore the ordinary artisan was well motivated to apply various analyses to detect antigen specific activation of T cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to select multi parametric flow cytometry analysis to determine antigen specific activation of T cells to a wide variety of antigens as a useful tool to analyze and characterize T cell immunity with a high degree of specificity and sensitivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

11. Claims 1, 3-6, 8-10 and 13-17 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-2, 4-8 and 9-15 of copending application Serial No. 08/760,447. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

12. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 2, 7, 11, 12, and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of copending application USSN 08/760,447. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are all essentially drawn to the same multi parametric flow cytometry analysis to determine antigen specific activation of T cells to a wide variety of antigens as a useful tool to analyze and characterize T cell immunity with a high degree of specificity and sensitivity .

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 2, 7, 11, 12 and 18 are directed to an invention not patentably distinct from claims 1-15 of commonly assigned USSN 08/760,447 for the reasons set forth above in section. .

Commonly assigned USSN 08/803,702, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

15. Claims 1-18 are provisionally rejected under 35 U.S.C. § 103 as being obvious over copending application Serial No. 08/803,702.

USSN 08/803,702 discloses essentially drawn to the same multi parametric flow cytometry analysis to determine antigen specific activation of T cells to a wide variety of antigens as a useful tool to analyze and characterize T cell immunity with a high degree of specificity and sensitivity as the instant application. USSN 08/803,702 differs from the instant application by not teaching lysing red cells in the preparation of T cells, however this was a long practiced procedure in the art at the time the invention was made. Also, USSN 08/803,702 differs by not teaching the use of immunosuppressive or immunoaugmenting drug either in vitro or in vivo, however such limitations would have been obvious either in terms of characterizing the T cell response in vitro or in terms of the treatment of patients undergoing analysis.

One of ordinary skill in the art at the time the invention was made would have been motivated to select multi parametric flow cytometry analysis to determine antigen specific activation of T cells to a wide variety of antigens as a useful tool to analyze and characterize T cell immunity with a high degree of specificity and sensitivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Copending application Serial No. 08/803,702 has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. § 102(e) if patented. This provisional rejection under 35 U.S.C. § 103 is based upon a presumption of future patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 C.F.R. § 1.132 that any unclaimed invention disclosed in the copending application was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention prior to the effective U.S. filing date of the copending application under 37 C.F.R. § 1.131.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014 or (703) 308-4242.

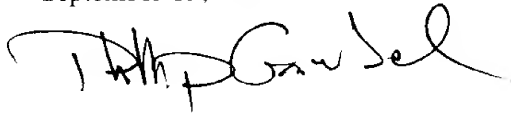
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Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [lila.feisee@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Phillip Gambel, Ph.D.  
Patent Examiner  
Group 1800  
September 15, 1997

A handwritten signature in black ink, appearing to read "Phillip Gambel", written in a cursive style.